

A Review on Research Guidelines for Evaluation of Safety and Efficacy of Herbal Medicine

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ABSTRACT

Herbal medicines have been used for centuries for the prevention and treatment of various diseases. However, the safety and efficacy of these natural products remain a concern due to the lack of rigorous scientific research. This paper outlines guidelines for the evaluation of the safety and efficacy of herbal medicines. The guidelines include identifying the active constituents, defining the target, studying the mechanism of action, determining the dose-response relationship, conducting toxicity studies, studying the pharmacokinetics, conducting well-designed clinical trials, analyzing the results, and publishing the findings. These guidelines provide a framework for conducting rigorous scientific research on herbal medicines and promoting evidence-based use of these natural products. It is essential to follow these guidelines to ensure the safety and efficacy of herbal medicines and to promote the integration of traditional and modern medicine.

I. INTRODUCTION

Herbal medicine has been used for thousands of years to treat various ailments, and its use continues to grow in popularity today. However, there is a need for standardized guidelines to evaluate the safety and efficacy of herbal medicines. The development and implementation of research guidelines for evaluating the safety and efficacy of herbal medicine is crucial to ensure the quality and safety of these products and to promote their integration into mainstream healthcare.

Objective

The primary objective of research guidelines for the evaluation of safety and efficacy of herbal medicine is to ensure that herbal medicines are safe, effective, and of high quality.

These guidelines are intended to provide a standardized framework for the development and evaluation of herbal medicines, with the goal of increasing their acceptance and integration into mainstream healthcare.

The specific objectives of research guidelines for evaluating herbal medicine may include:

- i. Establishing a standardized approach to evaluating the safety and efficacy of herbal medicines.
- ii. Ensuring the quality and consistency of herbal medicines, including the botanical identity, preparation, chemical characterization, and labeling.

Goals

The goals of research guidelines for the evaluation of safety and efficacy of herbal medicine are to promote the development of safe, effective, and high-quality herbal medicines, and to provide a standardized framework for their evaluation. These guidelines aim to achieve the following goals:

- i. **Safety:** To ensure the safety of herbal medicines through the identification of potential risks and the evaluation of toxicity and adverse effects.
- ii. **Efficacy:** To assess the efficacy of herbal medicines through well-designed clinical trials and other research methods.
- iii. **Quality:** To ensure the quality and consistency of herbal medicines through the development of Good Manufacturing Practices (GMPs) and other quality assurance measures.

II. USING THE GUIDELINES

The guidelines for the evaluation of safety and efficacy of herbal medicine can be used by various stakeholders, including manufacturers, researchers, regulatory agencies, and healthcare practitioners. Here are some ways in which the guidelines can be

applied:

I. Development of herbal medicines:

Manufacturers can use the guidelines to develop high- quality herbal medicines that are safe and effective. They can follow the standardized approaches for botanical identification, preparation, chemical characterization, and labeling, as well as comply with regulatory requirements and quality assurance measures.

II. Evaluation of herbal medicines: Researchers can use the guidelines to evaluate the safety and efficacy of herbal medicines through well-designed clinical trials and toxicity studies. They can also use the guidelines to identify potential risks and adverse effects of herbal medicines.

III. Regulation of herbal medicines: Regulatory agencies can use the guidelines to develop and enforce regulations for the development, evaluation, and marketing of herbal medicines. They can also use the guidelines to evaluate the quality, safety, and efficacy of herbal medicines.

Guidelines for quality specifications of plant material and preparations

The guidelines for quality specifications of plant material and preparations provide a framework for ensuring the quality and consistency of herbal medicines. These guidelines are an important component of the overall research guidelines for the evaluation of safety and efficacy of herbal medicine. Here are some key aspects of the guidelines:

- **Botanical identification:** The guidelines provide criteria for the botanical identification of the plant material used in herbal medicines. This includes using validated botanical names, establishing the correct plant part used, and verifying the identity through macroscopic and microscopic analysis.
- **Quality parameters:** The guidelines specify the quality parameters for herbal medicines, including purity, strength, and composition. This includes establishing minimum and maximum levels for active ingredients, impurities, and contaminants.
- **Analytical methods:** The guidelines provide guidance on the analytical methods used to measure quality parameters of herbal medicines. This includes validated methods for identifying and quantifying active ingredients, as well as methods for detecting impurities and

contaminants.

- **Good manufacturing practices (GMPs):** The guidelines outline the GMPs for the production of herbal medicines, including the use of appropriate facilities, equipment, and personnel, and the establishment of standard operating procedures for production, testing, and documentation.
- **Labeling requirements:** The guidelines specify the labeling requirements for herbal medicines, including the common name, botanical name, plant part used, and the quantity and strength of active ingredients.
- **Documentation:** Record all relevant information about the plant materials and preparations, including their origin, cultivation, harvesting, processing, and storage.

Guidelines for toxicity investigation of herbal medicines

Guidelines for toxicity investigation of herbal medicines provide a framework for assessing the potential toxic effects of herbal medicines. These guidelines are essential for ensuring the safety of herbal medicines and protecting public health. Here are some key aspects of the guidelines:

- i. **Study design:** The guidelines provide guidance on the study design for toxicity investigation of herbal medicines. This includes appropriate animal models, doses, and routes of administration.
- ii. **Identification of toxic effects:** The guidelines specify the parameters to be monitored in order to identify toxic effects. These include clinical signs, mortality, body weight changes, hematology, clinical chemistry, and histopathology.
- iii. **Duration of study:** The guidelines provide recommendations on the duration of toxicity studies, which will depend on the intended use of the herbal medicine.
- iv. **Selection of doses:** The guidelines provide guidance on the selection of doses to be used in toxicity studies. This includes the use of both high and low doses to identify potential toxicity at both ends of the dose-response curve.
- v. **Evaluation of results:** The guidelines provide guidance on the evaluation of study results. This includes the interpretation of clinical and laboratory findings and the establishment of

safe exposure levels

Guidelines for Pharmacodynamics and General Pharmacological Studies of Herbal Medicines –

Pharmacodynamics is the study of how drugs or medicinal substances interact with the body at the molecular, cellular, and physiological levels. Herbal medicines are natural products that have been used for centuries for the prevention and treatment of various diseases. Here are some general guidelines for conducting pharmacodynamic and pharmacological studies of herbal medicines:

- I. Identify the active constituents:** Identify the active constituents in the herbal medicine, which may be one or more compounds responsible for the pharmacological effect.
- II. Define the target:** Define the target or the receptor to which the active constituents bind and produce the desired therapeutic effect.
- III. Study the mechanism of action:** Investigate the mechanism of action of the herbal medicine by studying its effects on the target receptor, signaling pathways, and gene expression.
- IV. Determine the dose-response relationship:** Determine the dose-response relationship by administering different doses of the herbal medicine and observing the effect on the target receptor or physiological response.
- V. Conduct toxicity studies:** Conduct toxicity studies to determine the safety and toxicity of the herbal medicine in vitro and in vivo.
- VI. Study the pharmacokinetics:** Study the pharmacokinetics of the herbal medicine to determine its absorption, distribution, metabolism, and elimination from the body.
- VII. Conduct clinical trials:** Conduct well-designed clinical trials to evaluate the efficacy and safety of the herbal medicine in humans.
- VIII. Analyze the results:** Analyze the results of the studies to determine the pharmacodynamic and pharmacological properties of the herbal medicine and its potential clinical applications.
- IX. Publish the findings:** Publish the findings of the studies in peer-reviewed journals to disseminate the knowledge to the scientific community and to promote evidence-based use of herbal medicines.

III. GENERAL CONSIDERATIONS IN HERBAL MEDICINE RESEARCH

Legal consideration

When conducting research on herbal medicine, it is important to follow legal considerations and guidelines to ensure the safety and efficacy of the product. Here are some key legal considerations to keep in mind:

- 1. Regulatory Framework:** Different countries have different regulatory frameworks for herbal medicines. In the United States, the Food and Drug Administration (FDA) regulates herbal supplements under the Dietary Supplement Health and Education Act (DSHEA). In Europe, herbal medicines are regulated under the Traditional Herbal Medicinal Products Directive (THMPD). Before conducting research, it is important to understand the regulatory framework in your country and comply with any relevant regulations.
- 2. Good Clinical Practice (GCP):** GCP is an international standard for designing, conducting, recording, and reporting clinical trials. It provides guidelines for ensuring that the rights, safety, and well-being of trial subjects are protected, and that the data generated by the trial are reliable and credible.
- 3. Adverse Events Reporting:** Researchers must report any adverse events that occur during the study to the relevant authorities. Adverse events can include side effects or other unexpected health problems.

Ethical considerations

Herbal medicine has been used for thousands of years as a primary form of healthcare in many parts of the world. However, the safety and efficacy of herbal medicine have not always been scientifically evaluated, and in some cases, these medicines can have adverse effects on the human body.

When conducting research on the safety and efficacy of herbal medicine, it is important to consider the following ethical guidelines:

- 1. Risk-Benefit Assessment:** The potential risks and benefits of the herbal medicine being tested must be carefully evaluated before the research begins. The risks should be minimized as much as possible while maximizing the benefits for participants.
- 2. Protection of Human Rights:** All research on herbal medicine should be conducted in

accordance with the principles of human rights, including the right to life, dignity, and privacy. Researchers must respect the rights and welfare of all participants involved in the study.

3. **Reporting of Results:** Researchers must report their findings in a clear, accurate, and transparent manner. This includes reporting both positive and negative results, as well as any adverse effects observed during the study.

Research approaches

There are several approaches and guidelines for evaluating the safety and efficacy of herbal medicine. Some of the most common ones include:

1. **Evidence-based approach:** This approach involves reviewing the available scientific literature on the safety and efficacy of the herbal medicine in question. This includes both pre-clinical and clinical studies, as well as any case reports or anecdotal evidence.
2. **Toxicological approach:** This approach involves assessing the potential toxicity of the herbal medicine in question, including any potential adverse effects on the liver, kidneys, or other organs. This may involve both in vitro and in vivo studies, as well as toxicity testing in animals.
3. **Pharmacological approach:** This approach involves assessing the potential pharmacological effects of the herbal medicine in question, including its potential mechanisms of action, pharmacokinetics, and pharmacodynamics. This may involve both in vitro and in vivo studies, as well as clinical trials.
4. **Regulatory guidelines:** There are several regulatory guidelines and frameworks that may be used to evaluate the safety and efficacy of herbal medicines, including the World Health Organization's guidelines on herbal medicines, the European Medicines Agency's guidelines on herbal medicinal products, and the United States Pharmacopeia's dietary supplement verification program.

Regulatory requirement

Herbal medicines are widely used globally for various health conditions, and their use is increasing rapidly. However, because they are not regulated like pharmaceutical drugs, there are concerns about their safety and efficacy. To address these concerns, regulatory bodies in many countries have established guidelines for evaluating the

safety and efficacy of herbal medicines.

The following are some of the regulatory requirements for research guidelines for the evaluation of safety and efficacy of herbal medicines:

1. **Preclinical studies:** Preclinical studies are required to evaluate the safety and efficacy of herbal medicines before human studies can begin. These studies usually involve testing the herbal medicine on animals to assess toxicity, pharmacological activity, and other relevant parameters.
2. **Clinical studies:** Clinical studies are required to evaluate the safety and efficacy of herbal medicines in humans. These studies are designed to determine the appropriate dose, safety, and efficacy of the herbal medicine. Clinical trials for herbal medicines follow the same guidelines and protocols as clinical trials for conventional drugs.
3. **Quality control:** Quality control is essential for herbal medicines to ensure their safety and efficacy: -Regulatory bodies require that herbal medicines are standardized, which means that their chemical composition is consistent and reproducible. This is necessary to ensure that the herbal medicine is safe and effective and to avoid the possibility of contamination or adulteration.

3.4 Purpose of research

The purpose of research evaluating the safety and efficacy of herbal medicine is to provide scientific evidence to support the use of herbal remedies in the prevention and treatment of various health conditions. Such research involves rigorous scientific studies that evaluate the pharmacological activity, toxicity, and therapeutic efficacy of the herbal product.

The findings from these studies are important for several reasons. Firstly, they help to establish the safety and efficacy of herbal remedies and provide guidance on the appropriate dosage and duration of treatment. This information can be useful for healthcare providers, patients, and regulators.

Secondly, research into herbal medicine can help to identify new active compounds that may have therapeutic potential for various health conditions. By understanding the mechanisms of action of these compounds, researchers can develop new drugs or improve existing ones.

Lastly, research into herbal medicine can help to preserve traditional knowledge and

practices related to the use of plants for healing. By documenting and validating the therapeutic properties of traditional herbal remedies, researchers can help to ensure that this valuable knowledge is not lost over time.

IV. CLINICAL RESEARCH OF HERBAL DRUG

Clinical research on herbal medicines is an important area of investigation, and guidelines for evaluating the safety and efficacy of these products are essential. These guidelines should include recommendations for study design, patient selection, and outcome measures, as well as considerations for other types of research. By following these guidelines, we can ensure that herbal medicines are used safely and effectively in clinical practice.

Protocol Preparation: - The preparation of protocols for the evaluation of safety and efficacy of herbal medicine involves several guidelines that are recommended to ensure the scientific rigor and ethical standards of the research. Here are some general steps that can be followed:

1. Define the research question: Clearly state the research question, the objectives of the study, and the hypothesis that will be tested.
2. Review the literature: Conduct a thorough review of the available literature on the herb or herbal medicine being studied. This will help to identify the potential risks, benefits, and possible interactions with other medications.
3. Select study population and sample size: Define the study population, inclusion and exclusion criteria, and sample size. The sample size should be sufficient to detect meaningful differences and minimize the risk of type I and type II errors.
4. Develop study interventions: Develop the herbal interventions that will be studied, including the dosages, frequency, and duration of treatment.

Clinical trial using herbal medicine: -

Clinical trials using herbal medicines for research should follow guidelines for the evaluation of safety and efficacy of herbal medicines. Here are some general guidelines that are typically followed:

1. Ethical considerations: Clinical trials must be conducted in an ethical manner, and participants should be informed of the risks

and benefits of participating in the trial.

2. Selection of participants: Participants should be selected based on specific criteria, such as age, gender, and medical history. Inclusion and exclusion criteria must be clearly defined to ensure that the participants are representative of the population being studied.
3. Randomization and blinding: Clinical trials should use randomization and blinding to minimize the risk of bias. Randomization ensures that participants are assigned to treatment groups in a random manner, while blinding ensures that neither the participants nor the researchers know which treatment is being administered.
4. Study design: The study design should be appropriate for the research question being investigated. For example, a randomized controlled trial is typically used to investigate the efficacy of a herbal medicine.
5. Intervention: The herbal medicine being investigated should be standardized to ensure consistency in dosage and quality.
6. Outcome measures: Outcome measures should be clearly defined and validated to ensure that they are reliable and accurate.
7. Safety monitoring: The safety of participants should be monitored throughout the trial, and adverse events should be reported.
8. Data analysis: Data should be analyzed using appropriate statistical methods, and the results should be reported in a transparent manner.
9. Reporting: The trial should be reported according to established guidelines, such as the Consolidated Standards of Reporting Trials (CONSORT) statement.

Phases of clinical trial: -

Clinical trials for herbal medicine generally follow the same basic phases as clinical trials for other types of drugs. These phases are:

Phase 1: This phase typically involves a small group of healthy volunteers who receive the herbal medicine to determine its safety, toxicity, pharmacokinetics, and pharmacodynamics.

Phase 2: This phase involves a larger group of patients who have the condition that the herbal medicine is intended to treat. The purpose of this phase is to evaluate the efficacy of the herbal medicine, as well as to further assess its safety and optimal dosing.

Phase 3: This phase involves a larger number of patients and is designed to confirm the efficacy and

safety of the herbal medicine in a real-world setting. This phase also involves randomized, double-blind, placebo-controlled studies to provide the strongest evidence of efficacy and safety.

Phase 4: This phase occurs after the herbal medicine has been approved for marketing by regulatory agencies, and involves continued monitoring of its safety and efficacy in a larger population.

Non-clinical studies: -

Non-clinical studies are preclinical investigations of herbal medicines that are conducted in vitro or in vivo, usually in laboratory animals or cell cultures, to evaluate the safety and efficacy of the product before testing it in human subjects.

The guidelines for the evaluation of safety and efficacy of herbal medicines may vary depending on the regulatory requirements of the country or region where the product is being developed or marketed. However, some general principles that are commonly followed in non-clinical studies for herbal medicines include:

10. Toxicology studies: These studies are conducted to evaluate the safety of the herbal medicine by assessing its potential toxicity and side effects. Toxicology studies may include acute toxicity testing, repeated dose toxicity testing, and genotoxicity testing.
11. Pharmacology studies: These studies are conducted to evaluate the efficacy of the herbal medicine by assessing its pharmacological activity, such as its effects on various physiological systems or biomarkers. Pharmacology studies may include in vitro studies on cellular models or in vivo studies on animal models.
12. Pharmacokinetic studies: These studies are conducted to evaluate the absorption, distribution, metabolism, and excretion (ADME) of the herbal medicine in the body. Pharmacokinetic studies may include in vitro studies on cellular models or in vivo studies on animal models.
13. Stability studies: These studies are conducted to evaluate the stability of the herbal medicine under various storage conditions, such as temperature, humidity, and light exposure.
14. Formulation studies: These studies are conducted to evaluate the optimal formulation of the herbal medicine for maximum efficacy and safety.

5. Advantage of research guideline of evaluation of safety and efficacy of herbal medicine:

Research guidelines for the evaluation of safety and efficacy of herbal medicine have several advantages, including:

1. Standardization: Research guidelines help to standardize the evaluation process, ensuring that studies are conducted in a consistent manner. This reduces the potential for bias and increases the reliability of the results.
2. Safety: Guidelines help to ensure that studies are conducted with appropriate safety measures in place. This can include requirements for the reporting of adverse events, as well as guidelines for the dosage and administration of herbal medicines.
3. Efficacy: Guidelines can help to ensure that studies are designed in a way that allows for the evaluation of efficacy. This can include requirements for the use of appropriate controls, as well as guidelines for the selection of outcome measures.
4. Transparency: Guidelines can help to increase transparency in the research process, ensuring that all relevant information is reported and that studies are conducted in an ethical manner.
5. Recognition: Guidelines provide a framework for the evaluation of herbal medicines that is recognized by regulatory agencies and other stakeholders. This can help to facilitate the approval and acceptance of herbal medicines as safe and effective treatments.

V. CONCLUSION

- In conclusion, the evaluation of safety and efficacy of herbal medicine requires a rigorous and systematic approach that takes into account various factors such as botanical identification,
- Quality control of raw materials, standardization of herbal preparations, stability testing, and compliance with regulatory requirements. When conducting pharmacodynamic and general pharmacological studies, researchers should choose appropriate animal models, determine the optimal dose range, use appropriate study designs, and select outcome measures that are relevant to the condition being treated. Similarly, when investigating the potential toxicity of herbal medicines, researchers

should choose appropriate animal models, conduct clinical observations, and biochemical and histopathological analysis, and evaluate the safety of the herbal medicine.

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